REMARKS

Claims 2 and 3 were previously cancelled. Claims 4-10 were previously withdrawn. Applicants reserve the right to file continuation or divisional applications directed to the cancelled and withdrawn subject matter. Claim 1 is currently under consideration.

Rejection Under 35 U.S.C. §112, First Paragraph

Claims 1 is rejected under 35 U.S.C. §112, first paragraph as failing to comply with the written description requirement. The Examiner states that there is no support in the application for a method of inducing SIDR to glomular nephritis using the method steps recited in the claim. The Examiner states:

> Previously pending claim 3 discloses the claimed method wherein *streptococcus is the causative agent for glomerular nephritis*. However, claim 1 encompasses the treatment of glomerular nephritis wherein streptococcus is not the causative agent and there is no support for said method in the specification as originally filed. There is no support for the scope of the claimed invention in the specification as originally filed (aka the claimed invention constitutes new matter).

(Emphasis in original). See Office Action at page 2, paragraph 2.

35 U.S.C. §112, first paragraph requires that a specification enable one skilled in the art to make and use the claimed invention. A specification fails to meet this requirement if the specification fails to provide sufficient information regarding the claimed subject matter to enable a skilled artisan to make and use the claimed invention. "However, to comply with 35 U.S.C. §112, first paragraph, it is not necessary to 'enable one of ordinary skill in the art to make and use a perfected, commercially viable embodiment absent a claim limitation to that effect.' CFMT, Inc. v. Yieldup Int'l Corp., 349 F.3d 1333, 1338, 68 USPQ2d 1940, 1944 (Fed. Cir. 2003)." (MPEP §2164). To determine if sufficient information is provided, one must inquire whether the claimed invention can be practiced without undue experimentation.
MPEP §2164.01. That some experimentation may be required is not fatal because the issue is whether the experimentation is undue. In re Vaeck, 20 USPQ2d 1438, 1444 (Fed. Cir. 1991).

Applicants respectfully traverse the rejection and assert that the claims are fully enabled.

The Examiner insists claim 1 encompasses the treatment of glomerular nephritis when streptococcus is not the causative agent. *Id.* at page 2, paragraph 2. Applicants respectfully contend that claim 1 does not require the further limitation that the subject suffering from glomerular nephritis must be affected with a streptococcal infection. As explained in detail in Applicants' previous response, treatment may be initiated without knowledge of the causative factor, even if one suspects that distinct causative agents may be responsible for development of a disease.

As an example, meningitis is commonly treated by administration of antibiotics prior to obtaining any information on the presence or absence of bacteria in the spinal fluid. Pneumonia is commonly treated with antibiotics regardless of whether the condition is caused by a viral or bacterial infection. Even when bacterial, antibiotic regimes are often altered or modified at a later point if the causative agent is determined to be a mycoplasma (also known as PPLO), which is resistant to the penicillin-type antibiotics. Antitubercular medicine is often administered to AIDS patients in cases of tuberculosis type symptoms. In contrast to non-HIV infected patients where *Mycobacterium tuberculosum* is the causative agent, tuberculosis in AIDS patients is often caused by opportunistic infection by related members of what are referred to as the MAI (*Mycobacterium avium* and *Mycobacterium intracellulare*) family. These cousins of *M. tuberculosum* differ from *M. tuberculosum* in that they are non-pathogenic to non-immune comprised patients. More importantly, they are immune to the standard TB drugs. Nonetheless, standard anti-tuberculosum drugs are administered prior to identification of the particular mycobacterium species (a process that may take months). This is due to the fact that a an individual infected with *M. tuberuculosum* is considered to be infectious while a patient with MAI is not considered to be infectious *per se* as these bacteria are commonly found in the environment.

In each of the cases described above, a standard method of treatment is used despite that fact that (1) the existence of multiple causative agents may affect the particular effectiveness of the treatment; and (2) the particular etiology of the disease condition will sometimes render the standard treatment ineffective. Thus, administration of antibiotics is considered to be a medically appropriate method of treatment of meningitis; administration of antibiotics is

considered to be a standard and effective method of treatment of pneumonia; and the administration of anti-TB drugs is a medically responsible method of treating a disease with tuberculosis symptoms in an AIDS patient. The fact that other causative agents may exist is not a bar to treatment based on a particular causative agent.

Therefore, the recitation of a method of treatment of glomerular nephritis does not impart a requirement for the determination of whether streptococcal infection is the causative agent of the medical disorder. The fact that a subject suffers from glomerular nephritis qualifies the subject a candidate for the presently claimed treatment. It is possible that a subject suffering from glomerular nephritis due to reasons other than streptococcal infection may not experience positive results from the claimed treatment. However, this does not render the presently claimed method inappropriate or unjustified.

Claim 1 recites a process for producing selective immune down regulation in a subject with rheumatic fever or glomerular nephritis comprising the administration of components or fragments of streptococcus bacteria. As described in detail above, Applicants clearly describe a method of treatment of glomerular nephritis in general. The fact that glomerular nephritis is usually caused by streptococcal infections is helpful in regard to predicting that positive benefits will be generated by this method. Claim 1 therefore satisfies the written description requirement of 35 U.S.C. § 112, first paragraph. Accordingly, Applicants respectfully request reconsideration and withdrawal the rejection.

Rejection Under 35 U.S.C. §103(a)

Claims 1-3 were rejected under 35 U.S.C. §103(a) as unpatentable over Chen *et al*., (WO 96/39176; hereinafter "Chen") in view of Katz (US Patent No. 4,950,469). The Examiner states:

> Chen et al. teach that oral tolerance to autoantigens can be used to treat antibody mediated autoimmune disease wherein the disease involves antibodies which bind the pertinent autoantigen (see claims 1-13, pages 12-14, 40, 41). Oral tolerance is a form of "selective immune down regulation" (see specification, page 17, second paragraph). Chen et al. do not teach that disease provoking antigen is streptococcus which is involved in the pathogenesis of rheumatic fever, Katz et al. teach that rheumatic fever involves an autoimmune antibody response caused by anti streptococcal

> antibodies which cross react with human tissues (see column 6, first paragraph). It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have created the claimed invention because Chen et al. teach that oral tolerance to autoantigen can be used to treat antibody mediated autoantigen whilst Katz teaches that teach that rheumatic fever involves an autoimmune antibody response caused by anti streptococcal antibodies which cross react with human tissue wherein the streptococcal antigens would function as an autoantigen

Id. at page 3, paragraph 4.

Applicants respectfully traverse the rejection. The recently revised Examiner guidelines for assessing obviousness set forth detailed requirements based on asserted rationales for obviousness. The Rationales To Support Rejections Under 35 U.S.C. §103 provide the following possible rationales:

> (A) Combining prior art elements according to known methods to yield predictable results;
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> (B) Simple substitution of one known element for another to obtain predictable results;
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> (C) Use of known technique to improve similar devices (methods or products) in the same way;
>
> (D) Applying a known technique to a known device (method or product) ready for improvement to yield predictable results;
>
> (E) "Obvious to try" – choosing from a finite number of identified, predictable solutions, with a reasonable expectation of success;
>
> (F) Known work in one field of endeavor may prompt variations of it for use in either the same field or a different one based on design incentives or other market forces if the variations are predictable to one of ordinary skill in the art; and
>
> (G) Some teaching, suggestion, or motivation in the prior art that would have led one of ordinary skill to modify the prior art reference or to combine prior art reference teachings to arrive at the claimed invention.

See MPEP 8th Edition, rev. 6, §2141.

Applicant proceeds with the understanding that this rejection conforms to rationale G quoted above. The MPEP further sets forth the requirements for an obviousness rejection under this rationale:

> To reject a claim based on [rationale G], Office personnel must resolve the Graham factual inquiries. Then, Office personnel must articulate the following:
>
> (1) a finding that there was some teaching, suggestion, or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings;
>
> (2) a finding that there was reasonable expectation of success; and
>
> (3) whatever additional findings based on the Graham factual inquiries may be necessary, in view of the facts of the case under consideration, to explain a conclusion of obviousness.
>
> The rationale to support a conclusion that the claim would have been obvious is that "a person of ordinary skill in the art would have been motivated to combine the prior art to achieve the claimed invention and that there would have been a reasonable expectation of success." DyStar Textilfarben GmbH & Co. Deutschland KG v. C.H. Patrick Co., 464 F.3d 1356, 1360, 80 USPQ2d 1641, 1645 (Fed. Cir. 2006). **If any of these findings cannot be made, then this rationale cannot be used to support a conclusion that the claim would have been obvious to one of ordinary skill in the art.** [emphasis added]

See MPEP 8th Edition, rev 6, §2143

The rationale to support a conclusion that the claim would have been obvious is that "a person of ordinary skill in the art would have been motivated to combine the prior art to achieve the claimed invention and that there would have been a reasonable expectation of success." DyStar Textilfarben GmbH & Co. Deutschland KG v. C.H. Patrick Co., 464 F.3d 1356, 1360, 80 USPQ2d 1641, 1645 (Fed. Cir. 2006). If any of these findings cannot be made, then this rationale cannot be used to support a conclusion that the claim would have been obvious to one of ordinary skill in the art. See MPEP 8th Edition, rev 6, § 2143.

Applicants respectfully contend that the combination of Chen in view of Katz does not render claim 1 obvious. The Examiner states that "Katz et al., teaches that rheumatic fever

involves an autoimmune response caused by anti streptococcal antibodies which cross react with human tissues." *Id.* at page 5, paragraph 4. However, Katz never acknowledges that fact that rheumatic fever is caused by an infection with streptococcus. In addition, there is no discussion in Katz of the possibility that rheumatic fever (or a similar condition) may be caused by direct administration of streptococcal proteins.

Chen does not remedy the deficiencies of Katz. Applicants again draw the Examiner's attention to the definition of the term "autoantigen" provided by Chen: "The term also includes antigenic substances that induce conditions having the characteristics of an autoimmune disease when administered to a mammal." (Emphasis added). Chen teaches the administration of the protein itself as sufficient to invoke an autoimmune response to host proteins. It was not naturally implicit to one of skill in the art at the time of filing the present application that administration of a foreign protein can mimic induction of an autoimmune response derived from production of that protein during a pathogenic infection. It was only after publication of the Quinn paper (and consequently, after the filing of the present invention) that the ability of streptococcal proteins to themselves invoke an autoimmune response was described. The title of the Quinn publication is instructive: "Induction of Autoimmune Valvular Heart Disease by Recombinant Streptococcal M Protein". It is clear that, at the time of the publication of the Quinn paper, the concept that streptococcal proteins could invoke an autoimmune response without the bacterial agent itself was new. Quinn summarized this idea in the Discussion section: "In addition, our **novel observations** in the Lewis rat show that streptococcal M protein induced valvular heart disease that resembled valve disease in RF." (Emphasis added). Prior to this publication there were no indications that streptococcal proteins could be administered to invoke an autoimmune response (in a subject) to the subject's own tissues. Consequently, streptococcal proteins were not known to fulfill the characteristics of the antigenic substances that were included in the Chen reference at the time of the filing of the present invention.

Thus, one of skill in the art would have no motivation to combine the teachings of Chen and Katz because neither reference teaches that streptococcal proteins could provoke an autoimmune antibody response. One would have no expectation that the combination would be effective because Applicants' invention is directed towards a process for producing selective

immune down regulation in a subject with rheumatic fever or glomerular nephritis comprising administering of components or fragments of streptococcus bacteria. Claim 1 is not rendered obvious by the combination of Chen and Katz. Withdrawal of the rejection is respectfully requested.

Conclusion

Applicants respectfully submit that all claims are in condition for allowance. Early notification of a favorable consideration is respectfully requested. In the event any issues remain, Applicants would appreciate the courtesy of a telephone call to their counsel at the number listed below to resolve such issues and place all claims in condition for allowance.

The Examiner is invited to contact the undersigned at 412-918-1100 to discuss any matter concerning this application.

The Office is hereby authorized to charge any additional fees or credit any overpayments under 37 C.F.R. § 1.16 or § 1.17 to the deposit account number 50-0525.

Respectfully submitted,

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